Neural Imaging of Visual Word Processing in Aphasia Patients

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***Abstract*—We use signal processing and statistical methods to investigate how the human brain electrically processes visual information. Using magnetoencephalography (MEG) measurements from normal subjects and aphasic patients, we compare how different current source localization methods influence our results. These methods are then used to observe and measure how the brain reacts to visually presented words and to localize a neural source for this activity. Finally, using pre- and post-therapy MEG data from aphasic patients, we investigate whether this therapy changes the neural processing of visual words and how it is different than that in a normal brain.**

***Index Terms*—aphasia, MEG, source localization, neuromagnetic**

I. Introduction

APHASIA is a cognitive disorder which impairs an individual's ability to understand or express language either in its written or spoken format. This disorder occurs when the language processing areas of the brain are damaged in some way [1]. In our investigation, we examine aphasia patients who have had a stroke resulting in damage to the language areas located in the left hemisphere of the brain.

Current therapeutic methods for aphasia involve retraining the patient to process language, and these methods concentrate on improving verb comprehension and manipulation, as this has been shown to be the most problematic issue in a majority of aphasia patients [2].

In the unpublished study that yielded the raw data for our analysis, Y. Shah conducted visually presented verb comprehension tests with a variety of verbs on four subjects. Two subjects had aphasia resulting from stroke-induced brain damage and two were control subjects. Magnetoencephalography (MEG) was used to record neural activity in the form of magnetic fields recorded at the head surface of these subjects during these tests. Magnetic Resonance Imaging (MRI) scans were also conducted on the two aphasic subjects to obtain structural and neuroanatomical information. Shah then administered speech and comprehension therapy to the two aphasic subjects and after a time space of one month, she tested the two subjects again while taking more MEG readings.

MEG recording is noninvasive and has a high time resolution. However, there is no direct and unique map between the MEG measurement and neural source location in the brain. To localize the neural source, an inverse problem has to be solved with biological constraints, e.g. the source location has to be on the surface of the cortex.

The goals of our analysis are to:

(1) use these MEG recordings and MRI scans to accurately localize which brain regions are involved in processing visually presented verbs.

(2) determine if there are quantifiable differences in brain response due to the effects of therapy in each patient.

(3) determine if there are quantifiable differences between aphasic and normal subjects in the MEG response to visually presented verbs.

There have been previous studies on verb comprehension in aphasic subjects using fMRI and electroencephalography (EEG), however the use of MEG and MRI assisted source localization is a relatively unexplored methodology.

II. Methods

A. Subjects

The MEG results of five subjects were used in this project. Three among them were normal healthy people while the other two were aphasia patients. One of the normal subject's data were excluded from the analysis due to an excess of environmental noise in the MEG recording. Thus, the analysis was based on four subjects, two normal and two aphasics. The experiment was conducted by the Hearing and Speech Sciences department at the University of Maryland.

B. Visual Stimuli

During the experiment, four different sets of stimuli were presented to the subjects. Each set contained 51 different words of the same condition and each word was shown to the subject for 300 ms, with the interval between two words being randomized between 2 and 3 seconds. The four different conditions of each set were as follows:

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Condition 1: Inflected words (eg. "riding", "pushing")
Condition 2: Pseudo inflected words (eg. "ridest", "pushest")
Condition 3: Pseudo words (eg. "drism", "zide")
Condition 4: Uninflected words (eg. "ride", "push")

The subjects were shown the words from these different conditions in a pseudorandom order and were asked to press a certain button if the word presented was real and a different button if it was a pseudo word.

C. *MEG Recording*

Subjects reclined horizontally in a magnetically shielded room. Visual stimuli were delivered by a series of optical projections to a screen above the patient's head on the ceiling, right at the natural line of sight of the reclining patient.

MEG recordings were then made to record neural activity in the form of magnetic fields recorded at the head surface during the visual word processing test conducted on these subjects.

MEG is noninvasive and has millisecond level temporal resolution necessary to our research. The particular unit used in the study was a 157-channel whole-head system (Kanazawa Institute of Technology, Kanazawa, Japan). Environmental magnetic interference is cancelled using three reference sensors in the system.

From this point, we used the MNE-Suite and Freesurfer software packages to apply statistical methods in developing a forward solution.

D. *Freesurfer and MNE-Suite*

Freesurfer utilizes MRI head scans to reconstruct the cortical surface for a 3-D visual display. MNE-suite uses the boundary element model (BEM) of the head to calculate the forward solution. Therefore, the first step in using MNE-suite to calculate the forward solution is to tessellate the Freesurfer generated surfaces separating regions of different electrical conductivities which consist of the inner skull, outer skull, and outer skin into triangular surface elements. These surfaces are generated using the watershed algorithm [3]. Next, MEG coordinates are aligned to MRI coordinates by visually identifying the fiducial landmark locations used in the MEG measurement process (One between the eyes on the bridge of the nose and, two each of points in front of the central portion of the ear) on a 3-D model of the head based on MRI coordinates.

At this point, MNE-suite uses a single-compartment BEM which assumes the shape of the intracranial volume based on the previous surface calculations and assigns the conductivity values to the BEM compartments: for the scalp and the brain compartments, the default is 0.3 S/m with the default skull conductivity set about 50 times smaller, at about 0.006 S/m. Finally, using this BEM, MNE-suite generates a model for calculating possible forward solutions within this realistic head model. The forward solution model is based on a discrete form of established tomographic reconstruction methods [4]:

$$b(t) = \sum_{n=1}^{N} L(r_n) s(r_n, t) \qquad (1)$$

b is the magnetic field measurement and L is a vector field for the forward solution (possible current source) based on a dipole solution, and s is the neural source strength. In terms more specific to our realistic head model this becomes,

$$b(t) = [L(r_1), \quad L(r_2), \quad \ldots. \quad L(r_N)] \begin{bmatrix} s(r_1,t) \\ s(r_2,t) \\ \vdots \\ s(r_N,t) \end{bmatrix} \qquad (2)$$

where the possible forward solution is represented by a composite lead-field matrix over all head model voxel locations and s is representative of source strengths at the voxel locations.

E. *Correlation Based Inverse Solution*

Finally, characterize the inverse solution by calculating the correlation between the MEG measurement and every forward solution. We visualize this map on the cortical surface reconstructed by Freesurfer.

III. RESULTS

A. *Data Summary*

The MEG response averaged over all stimuli is shown in Fig. 1, for one aphasia patient. In the response waveform, one can see two clear peaks that happen before 100 ms. A smaller but wider peak also appears between 250 and 450 ms.

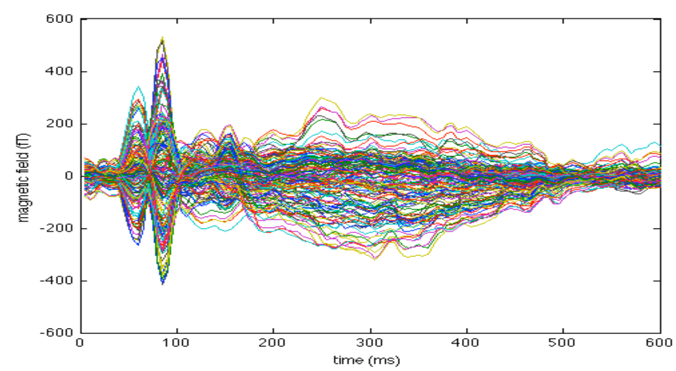

Fig. 1. An example of MEG waveform results for aphasic subject. This data is from aphasia patient R0655.

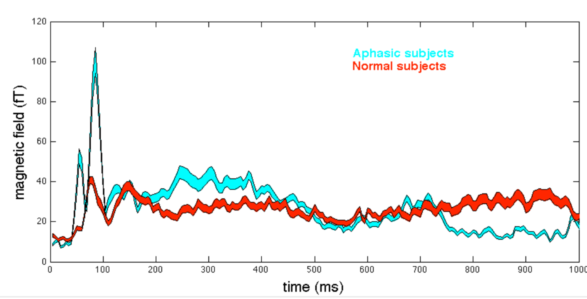

Fig. 2. Aphasic subjects waveform (cyan) versus normal subjects waveform (red).

In Fig. 2, both of the aphasic subject waveforms were grouped and the mean was calculated; this same procedure was also applied to the waveforms of both normal subjects. Two early peaks are found in the aphasic grouped waveform while only one early peak is detected for normal subjects. Also the early peak of the aphasic subjects is clearly higher and more coherent than that of the normal subjects.

B. *Localization Graphs*

We determined where and when the neural computation for visual word processing occurs in patients under pre and post therapeutic conditions in order to compare these conditions and translate significant differences in neural activity in the aphasia patients before and after therapy as quantifiable evidence of physiological beneficial change due to aphasia therapy.

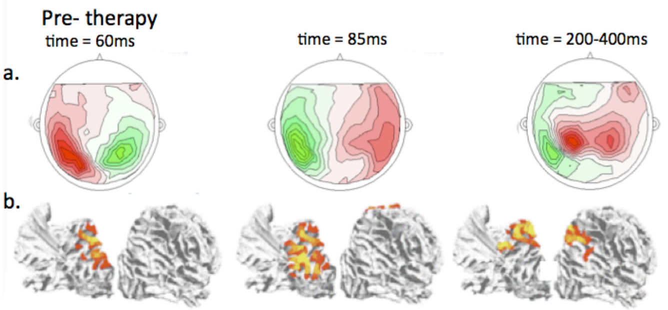

Fig. 3. a. Spatial distribution of magnetic field for aphasia patient R0655 (Pre therapy).
b. A back view from the brain showing the neural source localization. The color scale goes from red (weak source) to yellow (strong source)

In Fig.3, the peaks from Fig.1 are localized. The figures to the far left correspond to the first early peak at 65 ms, while the middle figures correspond to the second early peak at 90 ms. The figures at the far right are results from the late peak between 200 and 400 ms. In Fig. 3a. the spatial distribution of magnetic fields are plotted, which shows the active magnetic field regions based on the MEG results. As we can see from the far left pair of figures, the magnetic field is mostly centered in the back, the location of visual cortex. As a result, one can see in Fig. 3b. the neural source is found to be in the back of the head. However, in the last figure to the right the spatial distribution of the magnetic field is found to be in the left back corner. These results show that most of the strong sources are centered in the upper left side in the back of the brain

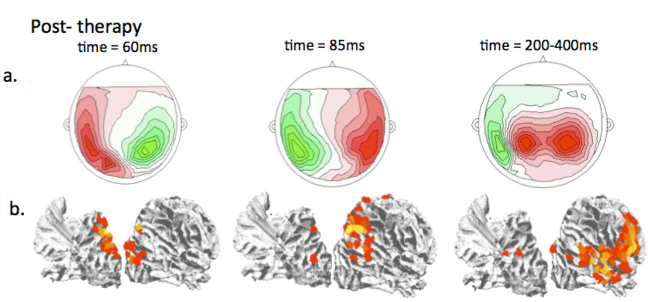

Fig. 4. a. Spatial distribution of magnetic field for aphasia patient R0655 (post therapy).
b. A back view from the brain showing the neural source localization. The color scale goes from red (weak source) to yellow (strong source)

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In Fig.4, a similar figure is shown for the same patient but this time the figure corresponds to the post-therapy MEG results. In these figures one can see that magnetic field is now lateralized more to the right than it was before therapy, especially in the middle and right images. As a result, neural sources are seen more to the right hemisphere than they were in the pre-therapy result.

Similar results were achieved when the data for the second aphasia patient (R0721) were analyzed. However, it was not possible to plot localization figure for the normal subjects because their MRI results were not obtained.

C. *Word Condition Comparison*

For each of the four subjects, a comparison test was made to see how much difference there is between any given pair of conditions (eg. inflected real word vs. pseudo word). This was done by taking the difference between the MEG responses of all iteratively paired conditions. If the difference was larger than twice of the standard error then a difference is detected. This procedure was done for each of the 157 sensors at each point in time (for 500 ms). This process was done six times for each subject corresponding to the differences between each of the four conditions.

Condition	Pseudo inflected	Pseudo	Uninflected
Inflected	729 (4.69%)	1857 (11.95%)	797 (5.13%)
Pseudo inflected		1501 (9.66%)	681 (4.38%)
Pseudo			1466 (9.43%)

Table. 1. differences between different word conditions for a normal subject. The number between the bracket is the percentage of difference data to the total number of trials.

Condition	Pseudo inflected	Pseudo	Uninflected
Inflected	599 (3.85%)	1270 (8.17%)	1075(6.92%)
Pseudo inflected		724 (4.66%)	638 (4.1%)
Pseudo			535 (3.44%)

Table. 2. differences between different word conditions for an aphasic subject. The number between the bracket is the percentage of difference data to the total number of trials.

Table 1 shows the number of differences between word conditions for each iterative pairing of conditions in one normal subject. One can see that the largest difference is between inflected words and pseudo words. Table 2 is a similar table, but for an aphasia subject. One can notice as well that the largest difference is between inflected words and pseudo words. If we add up the number of differences that appear in the normal subject graph, we get a total of 7031 differences, while in the aphasic subject only 4841 differences are yielded.

In order to visualize where the differences take place in the head, a spatial distribution of the magnetic field graph for each subject was taken as shown in Fig. 5. This graph shows the magnetic field distribution of the differences between inflected and pseudo words for both normal and aphasic subjects.

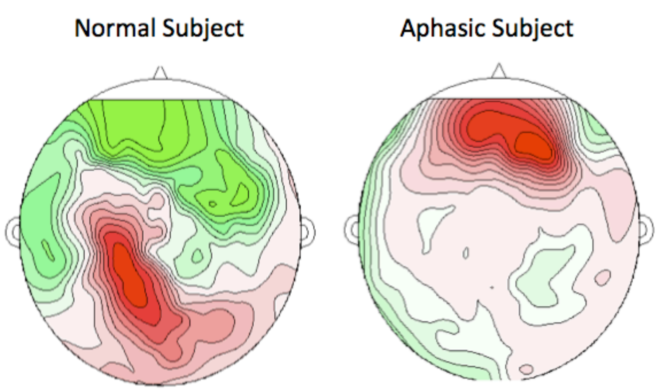

Fig. 5. Spatial distribution of the magnetic field for the differences between inflected words and pseudo words for a normal subject (left) and aphasic subject (right).

IV. Discussion

The MEG waveform results shown in Fig.2 are similar for all subjects in terms of the timing of the peaks. The difference is that the aphasic waveforms show higher peaks, which probably indicate that neural activity is stronger in aphasia patients. The two early peaks may be attributed to visual activities. The later peak (between 200-400 ms) indicates the word processing activity in the brain.

The localization results for pre- and post-therapy MEG measurements shows some differences in the source locations. This difference can be clearly seen in the figures at the far right in Fig. 3 and Fig. 4. These figures at the far right are the ones corresponding to the latest peak, which is thought to reflect word processing. In the post-therapy locations, the source is located mostly in the right hemisphere and not so much in the left as it previously was in pre-therapy.

This might be an indication that therapy helped aphasia patients to use their right hemisphere instead of their damaged left hemisphere, which is normally responsible for language processing. It might be the natural way for the brain to recover the damaged part by transferring the job to another region in the brain.

By looking at the tables of differences between different word conditions (tables 1 and 2), the largest difference can be seen between real inflected words (eg. "riding") and uninflected pseudo words (eg. "drism"). This makes sense because there are two differences between these words, in terms of real versus pseudo and in terms of inflected versus uninflected. The second largest difference is between pseudo inflected words and uninflected pseudo words, which probably means that whether a word is inflected or not is more different in brain processing than whether a word is real or pseudo.

Another observation one can draw from these tables is from the total number of differences in normal subjects versus aphasic subjects. From the data shown in the table and similar data taken from other subjects, normal subjects have many more differences between different word conditions than aphasic subjects. This is probably because normal people are better able to distinguish between the different types of words and as a result their brains show more differences in activity as is evident in the greater number of differences, which can be observed between the different word conditions than in an aphasic patient.

V. Conclusion

In aphasia patients, the MEG response to visual words is featured by an early and a late response component. By solving the inverse problem, we localized the early component, near 100 ms, to the visual cortex and the late component, near 300 ms, to the parietal cortex. Therapy in this case appears to have effected dramatic change within only the space of a month. The aphasia patients' shift in neural activity from the left to the right hemisphere indicates that a certain amount of adaptation has taken place and that word processing normally handled by the damaged area in the left hemisphere has been shifted to a part of the brain that is able to take over this function. We also were able to observe how a normal subject's brain shows a greater amount of difference in neural activity when distinguishing between words than an aphasia patient's brain. This would imply that the ability to apply therapy that increases differences in neural activity between the processing of different types of words would be a factor to consider when designing more effective types of therapy.

VI. Future Work

Further research into this topic would include an improvement on methods using MNE-suite: improving knowledge of the software so as to be able to effectively use the powerful inverse problem solving capabilities of MNE-suite. Obtaining a larger sampling group of both aphasia patients and normal control subjects would improve our analyses by making them more statistically robust. Other possible improvements could be made in our comparisons with the control subjects by obtaining MRI scans for all control subjects so that comparison of neural source localizations within realistic head models would be possible for all subjects and not just the aphasia patients.

Acknowledgment

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